The evolution of subjective cognition after meditation training in older people: A secondary analysis of the three-arm Age-Well randomized controlled trial

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Abstract

Aging is associated with cognitive changes, even in the absence of brain pathology. This study aimed to determine if meditation training, by comparison to active and passive control groups, is linked to changes in the perception of cognitive functioning in older adults. One hundred thirty-four healthy older participants from the Age-Well Randomized Clinical Trial were included: 45 followed a meditation training (age: 69.45 ± 3.70), 45 a non-native language training (age: 70.34 ± 4.50) and 44 had no intervention (age: 68.13 ± 2.76). Subjective cognition was assessed at baseline and following the 18-month intervention period. Perception of attentional efficiency was assessed using internal and external Attentional Style Questionnaire (ASQ) subscale scores. Perception of global cognitive capacities was measured via the total score of Cognitive Difficulties Scale (CDS). Deltas ([post-test minus pre-test scores] / standard deviation at pre-test) were calculated for the analyses. Generalized mixed effects models controlling for age, sex, education and baseline scores revealed that meditation training decreased the ASQ vulnerability score towards external distractors compared to non-native language training (estimate=-0.37, 95% CI: [-0.68,-0.05]), and no intervention (estimate=-0.34, 95% CI: [-0.66,-0.02]). However, no between-groups differences on ASQ internal or CDS total scores were observed. Results suggest a beneficial effect of meditation practice on perceived management of external distracting information in daily life. Meditation training may cultivate the ability to focus on specific information (e.g., breath) and ignore stimulation from other kinds of stimuli (e.g., noise).

Keywords: mindfulness; aging; attention; memory; cognitive training.

Introduction

With advancing age, individuals report an increasing number of cognitive, physical, and physiological complaints. In relation to cognition, older people perceived difficulties regarding memory functioning (usually working memory), but also for attention and executive processes which are highly correlated with memory problems in daily life (Newson & Kemps, 2006). Examples of daily life difficulties experienced by older people are remembering the name of a person just met or a phone number (Newson & Kemps, 2006), finding words (Martins, 2012), inattention or distraction to internal (e.g., thoughts) and external stimuli (e.g., noise, movement, etc.) (Langlois & Belleville, 2014). With aging, these perceived difficulties are also observed objectively through cognitive tasks with an impairment of episodic as well as working memory and a preservation of semantic, implicit as well as short-term memory processes (Harada et al., 2013; Verhaeghen et al., 2005). Among task-related attentional and executive difficulties, declining inhibitory ability is still debated. Inhibition refers to the ability to suppress or ignore irrelevant thoughts and actions (Logan, 1985), and is generally fractionated in specific subprocesses (see for example, Friedman & Miyake, 2004; Rey-Mermet & Gade, 2018), such as the ability to ignore distracting information, the ability to suppress dominant responses and resistance to interference. Based on the results of a meta-analysis (Rey-Mermet & Gade, 2018). Based on the results of a meta-analysis (Rey-Mermet & Gade, 2018), the suppression of dominant responses is most impacted by aging while older adults would perform similarly to young adults in their ability to ignore distracting information and response interference. . Discrepancies regarding the effect of age on interference sensitivity could also reflect recruitment of specific mechanisms according to task characteristics. For example, management of distraction can be related to both the susceptibility to be distracted (a bottom-up process) or the possibility to act (top-down process) on this distraction (Van Calster et al., 2018). Top-down processes are relatively preserved in aging, as opposed to bottom-up processes (Costello et al., 2010). Moreover, this interference sensitivity can be driven by both internal and external stimuli. For example, interference by internal stimuli refers to be distracted by thoughts (also called mind-wandering) or to be distracted by sensations and emotions. At the opposite, distraction by external stimuli is related to distraction towards movements or noise. There will be also divergent age effects according to the source of interference. For example, Maillet et al. (2020) showed that performance on a motor inhibition task is disproportionally affected in older versus younger adults by visual distraction but not by mind-wandering. Finally, most studies assessing sensitivity to external interference used distractors included in the task but, to our knowledge, only one study used unrelated task distractors (music sounds) and showed a negative impact on associative memory performance in aging (Reaves et al., 2016).

As mentioned above, the presence of age-related cognitive changes on memory, attentional and executive tasks is well attested through objective measures of performance (Collette, 2019b; Harada et al., 2013) but also through the complaints reported by older people (Steinberg et al., 2013) and both objective and subjective difficulties increase with age (Rabbit & Abson, 1991). However, subjective perception of difficulties is not always directly associated with objective cognitive performance (Zlatar et al., 2014). Indeed, rather than a similar evolution of subjective and objective difficulties through time, subjective perception of changes in cognition (measured by the Cognitive Difficulties Scale of McNair and Kahn (1983)) can predict the future decline in objective cognition (Dufouil et al., 2005). Accordingly, people experiencing subjective cognitive changes are at an increased risk of developing dementia (Rabin et al., 2017), especially when they seek professional help (Jessen et al., 2020). Regarding the absence of a similar evolution of subjective and objective difficulties through time (Zlatar et al., 2014), several explanations were proposed. For example, subtle declines may not be detected by common tests that can sometimes be not sensitive enough (Mcalister & Schmitter-

Edgecombe, 2017). Another explanation would be the presence of subclinical symptoms of anxiety associated with more cognitive decline and with an increased risk of dementia (Steinberg et al., 2013). One might therefore hypothesize that reducing cognitive complaints by reducing anxiety (and by increasing the accuracy of difficulties' perception) or by acting on subtle cognitive changes could be protective against future objective cognitive decline.

There is an important variability in the profiles of cognitive changes of older individuals, and the level of difficulties experienced in daily life may also be perceived as more or less disabling (Collette, 2019a). This variability may partly be explained by genetic and lifestyle characteristics and involvement in activities considered as protective according to cognitive reserve theories (e.g., Scaffolding Theory of Aging and Cognition of Reuter-Lorenz & Park (2014)). Among these activities, the practice of meditation has recently attracted a great deal of attention. Lutz et al. (2008) defined meditation as "a family of complex emotional and attentional regulatory training regimes developed for various ends, including the cultivation of well-being and emotional balance". Among styles of meditation, mindfulness which is related to open-presence and to attention towards sensations, and loving-kindness which is linked with positive attitudes toward others or oneself (Lutz et al., 2008). For example, Kirtan Kriya meditation (a multisensory practice based on mantras) has been shown to have a positive effect on cognitive complaints (Innes et al., 2017), and mindfulness traits were linked to a better suppression of intrusive thoughts in older adults (Erskine et al., 2017). In a recent model by Lutz et al. (2021), meditation practices were hypothesized to promote cognition, mental health, and well-being by strengthening attention control, metacognitive monitoring, emotion regulation and pro-social capacities, and as such could have a protective effect on Alzheimer's disease. Accordingly, we recently observed that 18 months meditation practice improved meta-cognitive monitoring and attentional control, but also socio-emotional abilities (Chételat et al., 2022).

We report here secondary outcome results from the 18-month Age-Well clinical trial to investigate whether meditation training improves perception of cognitive functioning in healthy older adults compared with an active control group (i.e., non-native language learning) and a no intervention group. Here, we hypothesized that at the end of the intervention period older adults in the meditation training group would report fewer cognitive complaints (assessed by the Cognitive Difficulties Scale; McNair & Kahn, 1983) and a better perceived management of distraction from internal and external stimuli (assessed by the Attentional Style Questionnaire; Van Calster et al., 2018), in comparison with the two control groups. In exploratory analyses, we also investigated the effect of variables related to dementia-risk (e.g., anxiety, depression, brain amyloid deposition, and apolipoprotein ε genotype) and variables related to the intervention (i.e., testing waves, practice, adherence, responsiveness, expectancy and credibility).

Method

Study design

The data presented were collected for the Age-well study of the Medit-Ageing project registered on ClinicalTrials.gov (NCT02977819). The detailed trial protocol was published in Poisnel et al. (2018).

Age-Well was a monocentric, observer-blind, randomized, controlled clinical trial with three parallel arms. Two arms were 18-month interventions of either meditation training or non-native (English) language training, while the third arm comprised a no intervention control group. There were three waves of recruitment that took place from November 2016 through March 2018. Participants were all seen at the laboratory of Cyceron (Caen, France) for a first screening. For those that met eligibility criteria, a first (baseline) visit was planned, during which behavioral, cognitive, biological and neuroimaging data were collected. Participants were then randomized (1:1:1) to one of the three arms: meditation training, non-native language training or no intervention. Neuropsychologists and neurologists responsible of pre- and post-data acquisition were blind to the group allocation. The same data were also acquired after 18 months (for a complete description of the data set acquired at each time point; see Poisnel et al., 2018).

Participants

All participants were cognitively healthy older adults, native French speakers, had at least seven years of education, and were retired for at least one year. They had to be free of neurological and psychiatric diseases with no history of drug misuse (for demographic characteristics, see *Table 1*). Detailed eligibility criteria have previously been reported (Poisnel et al., 2018). Shortly, the Montgomery and Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979) was used as an eligibility criterion, and participants who obtained a score above 7 were excluded. None of the participants reported recent history of neurological or psychiatric disease (including alcohol or drug abuse) or taking medication likely to affect the central nervous system. Finally, all obtained a score superior to 27 on the Mini Mental State Examination (Folstein et al., 2001). All participants gave their written informed consent to participate in the study and the research was completed in accordance with the declaration of Helsinki. The Age-Well clinical trial was approved by the ethics committee CPP (Comite de Protection des Personnes) Nord-Ouest III, Caen, France (EudraCT: 2016-002441-36; IDRCB: 2016-A01767-44).

[t]Table 1 near here[/t]

Experimental groups

The meditation and non-native language training interventions were structurally equivalent in overall course length, class time and home activities, and matched in administration, dosage, duration, and level of expertise and number of facilitators per class.

Meditation training

During the intervention, participants joined a 2-hour group session once a week, attended a 5-hour retreat day and were also instructed to complete daily exercises at home for at least 20 minutes. During the first nine months, mindfulness was the central topic and the last nine months, compassion meditation was taught. Mindfulness, or attentive presence, consists of cultivating a vigilant awareness of one’s own thoughts, actions, emotions and motivations. Participants learn to intentionally pay attention to their internal and external experiences in the present moment. The practice of loving kindness and compassion aims at promoting feelings of benevolence and care towards oneself and others. The program was facilitated by two meditation experts and contained sitting, walking, and group meditation practices (for details see Poisnel et al., 2018).

Non-native language training

The non-native language training intervention was structurally matched to the meditation training and comprised English lessons for two hours per week, a day on the Channel Island of Jersey and they were asked to engage with daily exercises at home for a least 20 minutes. The program was delivered by an American PhD student and an English teacher and was composed of oral comprehension and expression exercises (for details see Poisnel et al., 2018).

No intervention

Participants in the no intervention arm were asked to pursue their daily life activities as usual and were instructed not to engage in any meditation or English practices.

Behavioral assessment

Our variables of interest were scores obtained from the Cognitive Difficulties Scale (McNair & Kahn, 1983) and the Attentional Style Questionnaire (Van Calster et al., 2018). Scores from both self-report questionnaires reflect participants' subjective perception of their cognitive functioning (raw data in *Table 2*). The data were collected before the intervention and after 18 months (end of intervention for the two active groups).

[t]Table 2 near here[/t]

The Cognitive Difficulties Scale (CDS) is used to assess perceived cognitive difficulties in aging populations (McNair & Kahn, 1983). The questionnaire is composed of 39 statements that assess memory, language difficulties, spatiotemporal orientation, attention/concentration, and praxis (Cronbach's $\alpha > 0.850$) (Gass et al., 2020). Examples of items are as follows: "I have trouble recalling frequently used phone numbers" or "I put things down (glasses, keys, wallet, purse, papers) and have trouble finding them" (McNair & Kahn, 1983). Participants were asked to indicate presence of cognitive difficulties on a 5-point Likert scale ranging from 0 ("never") to 4 ("very often"). The total score (range: 0-156) corresponds to the sum of scores on the 39 items, with higher values representing more cognitive complaints.

The Attentional Style Questionnaire (ASQ) is composed of 12 items that can be grouped together in two subscales associated with internal (7 items, Cronbach's $\alpha = 0.79$) and external attention (5 items, Cronbach's $\alpha = 0.76$) (Van Calster et al., 2018). The internal attentional score is related to the sensitivity towards internal stimuli, such as thoughts, that can divert a person from a task completion (for example: "In general, I stay in control of my thoughts and do not let myself get distracted by interfering thoughts") and the external attentional score to the vulnerability towards external distractors such as music or movements (for example: "I have trouble concentrating when there is movement in the room I am in.") (Van Calster et al., 2018). Participants responded on a 6-point Likert scale that ranged from 1 ("totally disagree") to 6 ("totally agree"). For both scores (ranges: 7-42 and 5-30 respectively), higher values represent worse ability to cope with distracting information. A total score corresponding to the sum of both subscales (internal and external scores) may also be computed but was not used in the analyses.

Additional measures

Clinical characteristics from baseline assessment were considered in the exploratory analyses such as brain amyloid load (standard uptake value ratios were acquired with Florbetapir-PET late acquisition) and apolipoprotein (APOE) genotype (distinction between ε4 positive and ε4 negative). Further, measures directly associated with the interventions were also considered. The credibility of the intervention and expectations about its potential benefits were assessed in the two experimental groups after the first practice session with the Credibility and Expectancy Questionnaire from Devilly and Borkovec (2000).

We were also interested in waves in which participants were included, adherence (number of classes attended), practice (number of hours spent engaging in intervention activities of intervention sessions and at home), and responsiveness to the intervention. Two scores were used to assess responsiveness: a binomial categorical one (based on one question on the intervention benefit on the participant perceived by teachers and assessed on a Likert-scale from 0 "not at all" to 5 "a lot" for both groups and, in addition for the non-native language training group, on an English test, this score making the distinction between responders and non-responders, see Appendix I for more information) and a continuous score (based on a question on participants' evolution rated by the teacher and also, for the meditation group, self-perception of benefits reported by participants as well as meditation questionnaires, and for the English training group on improvement score on an English test). Finally, we were interested in anxiety and depression levels (State-Trait Anxiety Inventory, trait version (STAI B, Spielberger et al., 1970) and the Geriatric Depression Scale (GDS; Yesavage, 1988), respectively).

The raw data are reported in *Table 3* for each group separately and details about the additional measures can be found in Supplementary data (*Appendix II*). Moreover, raw data of anxiety and depression at baseline can be retrieved in Supplementary data (*Supplemental Table 1*).

[t]Table 3 near here[/t]

Power analysis

Age-Well was powered to detect an effect size of 0.75 for the trial's coprimary outcomes (i.e., volume and perfusion of the anterior cingulate cortex and insula), with 80% power and a 2-sided type I error of 1.25% (Poisnel et al., 2017). This resulted in a minimum of 126 participants (42 per arm), which was exceeded (137 total participants). Following guidance (Zang et al., 2019), post-hoc power analyses were not performed for this secondary outcome study.

Data analyses

Data were statistically analyzed with SAS 9.4 for Windows (SAS Institute Inc., 2013, https://www.sas.com). Results with two-sided $p < .05$ were considered as statistically significant.

Differences between groups on variables related to the intervention

Between-group differences for variables related to the intervention (adherence, practice, responsiveness, credibility, and expectancy) were computed with Mann-Whitney tests (PROC NPAR1WAY wilcoxon), as these variables were not normally distributed (PROC UNIVARIATE normal). For the categorical variable (responsiveness categorical score), Fisher exact test was used. As effect size, we reported the biserial correlations for metric variables and the Cramer's Phi for categorical variables.

Core models

To assess change in perception of cognitive functioning, delta scores ([measurement after 18 months minus first visit] / standardized deviation at baseline) were created for our three measures of interest: (total score of the Cognitive Difficulties Scale, internal and external scores of the Attentional Style Questionnaire). As there is no known cut-off to interpret the evolution of the variable, we divided the change score by the standard deviation of the whole sample on the baseline score. This allowed us to study the average evolution of the score in relation to its dispersion at inclusion. Lower delta scores correspond to perception of higher cognitive functioning after 18 months. Participants with one missing data at baseline (for internal and external scores: n=1 in meditation group and n=1 in control group) or post-intervention (n=1 in the control group, see *Table 2*) were not included in the analyses

Generalized mixed effect models (PROC GLIMMIX), with participant-level random intercepts, estimated via restricted maximum likelihood, were tested on the delta of each outcome variable: the total score of the CDS and the internal and external scores at the ASQ. The model used trial arms (i.e., 3 arms: meditation training, non-native language training, and no intervention) as predictors and was adjusted for age, sex, education and outcome baseline score. For each model, the semi-partial R-square (R_{sp}^2) is referenced when a significant effect was found and Tukey post-hoc tests conducted to investigate pairwise associations (LSMEANS statement). The adjusted p-values for multiple comparisons were reported. Changes over time for subjective perception of cognitive functioning were also assessed in each group with paired t-tests (PROC TTEST) with False Discovery Rate (p_{FDR}) correction (controlling for multiple comparisons) to see if between groups difference was explained by stable, increased or decreased performance over time in the comparators.

Exploratory analyses with risk factors and variables related to the intervention

Firstly, sensitivity analyses were performed using the same analyses as our core models (with the three groups as predictors and demographics as well as baseline score of the questionnaire as covariates) but here i) anxiety or ii) depression change over time (delta scores computed in the same way as for subjective cognitive scores) were added as an additional predictor; iii) participants in the intervention groups with adherence < 20% were removed; and iv) intervention non-responders were excluded (based on the responsiveness's categorical score).

Secondly, we employed mixed effect models for exploratory analyses on our deltas for each intervention group (meditation training and non-native language training) separately with different predictors: APOE4 status, amyloid level, credibility, expectancy, waves, adherence, responsiveness (continuous score) and practice score. All models were controlled for age, sex, education and baseline subjective cognition score.

Results

Out of 157 participants who attended a screening visit, 137 were randomized to meditation training (n=45), non-native language training (n=46), or no intervention (n=46). The Trial Steering Committee excluded two participants from all secondary analyses for not meeting eligibility criteria (i.e., history of head trauma and amyotrophic lateral sclerosis diagnosis after V2 [with a likely subclinical state at inclusion]). A total of 135 participants (age range: 65-84) were therefore included (Figure 1 and Table 1). One non-study-related death (myocardial infarction) was reported at follow-up and was therefore not included in the analyses. One participant did not follow their allocated arm (randomized to no intervention but attended non-native language training) and was analyzed within the non-native language training arm. The flowchart for the recruitment and randomization of participants is presented in *Figure 1*.

Differences between groups on variables related to the intervention

No differences between the two intervention groups were found regarding responsiveness categorical score (p=.16, φ_c=.185), adherence (p=.25, r_{pb}=*.14*), responsiveness practice (p=.79, r_{pb}=*.03*), credibility (p=.30, r_{pb}=*.13*), and expectancy measures (p=.34, r_{pb}=*.12*) (see Table 3).

Core models

Generalized mixed effect model did not demonstrate differences between our three groups (meditation training, non-native language training and no intervention) for changes in the CDS total score and in the internal score of the ASQ. However, differences were observed on changes in the external score of the ASQ (p<.01, R_{sp}^2=.07; *Figure 2*). The Tukey post-hoc tests showed a lower delta score (decreased vulnerability towards external distractors**)** in the meditation training arm compared to the non-native language training (estimate = -0.37, Tukey-Kramer adjusted 95% CI = [-0.69,-0.05], Tukey-Kramer adjusted p-value=.02) and the no intervention (estimate = -0.34, Tukey-Kramer adjusted 95% CI = [-0.66,-0.02], Tukey-Kramer adjusted p-value=.03) arms. There was no significant difference on the ASQ external score between non-native language training and the no intervention arm (estimate = 0.03, Tukey-Kramer adjusted 95% CI = [-0.31,0.36], Tukey-Kramer adjusted p-value=.98) (*Table 4*).

Moreover, assessment of changes over time (from baseline scores to post-intervention scores) for CDS and ASQ scores in each group with paired t-tests revealed a statistically significant difference in the meditation group only, with a reduction in the perception of external stimuli distraction from pre- to post-test (estimate = 1.64, 95% CI = [0.60,2.67], t(43)=3.18, *p*=.003, p_{FDR} = .02). The other scores (CDS and ASQ internal score) did not significantly differ from pre- to post-test (*ps*>.05) showing a relative stabilization of the scores over time in each group (*Table 4*).

[t]Table 4 near here[/t]

Exploratory analyses with risk factors and variables related to the intervention

The inclusion of anxiety delta score or depression delta score as an additional covariate, and exclusion of participants who attended less than 20% of intervention classes (only one participant removed) did not substantively affect any results (*Supplemental tables 2-3*). However, even if the analyses on the subsamples with the exclusion of non-responders still showed a group effect on the ASQ external delta score (*p*=02, R_{sp}^2=.06), there was only a significant better management of external stimuli in the meditation training group compared to non-native language training group (estimate = -0.36, Tukey-Kramer adjusted 95% CI = [-0.70,-0.02], Tukey-Kramer adjusted *p*-value=.04), but only a trend compared to no intervention (estimate = -0.34, Tukey-Kramer adjusted 95% CI = [-0.68,0.002], Tukey-Kramer adjusted *p*-value=.05) (*Supplemental table 2*).

For the second set of exploratory analyses, the results are presented separately for meditation training and for non-native language training (*Supplemental table 3*). For the meditation training group, there was an effect of baseline amyloid burden on CDS delta scores (higher amyloid is linked to higher cognitive complaints through time). For the non-native language training group, there was an effect of expectancy on ASQ internal delta scores (higher expectancy in the intervention linked to higher perceived distraction through time).

Discussion

The aim of this study was to examine whether changes in the perception of cognitive functioning are observed following 18-month meditation training compared to 18-month non-native language training or to no intervention. We observed changes in subjective perception of attentional style for the management of external distractions following meditation training compared with the other conditions. No between-group differences in changes in perceived management of internal distractions or perception of global cognition were observed. More precisely, the observation of the evolution of the subjective cognitive scores in each group showed a better management of external stimuli across time only in the meditation group while the other groups remain stable on all other measures.

After 18 months, the meditation training group reported less distraction by external stimuli (e.g., music, noise in the room) compared to both control groups (i.e., non-native language training and no intervention). However, the effect size is small and more studies are needed to support this result. This finding is consistent with the targets of mindfulness and compassion-based meditation practices taught during the intervention: these practices aim at strengthening the capacities to flexibly regulate attention and to monitor endogenous (e.g., thoughts), or exogenous (e.g., noise around) distractions without being carried away or bothered by them. Following this line of reasoning, it is unexpected that we found no beneficial effect of meditation practice on the perceived cognitive difficulties and on the perceived management of bodily feelings or thoughts. We tentatively propose that meditation practice may first improve tolerance to interference for external stimulation in novice older people. Indeed, meditation practice requires focusing on internal sensations such as breathing and not being impacted by the external world and thoughts (Kabat-Zinn, 2015). Older adults tend to be less ruminative or anxious compared to young people (Urry & Gross, 2010; Wuthrich et al., 2015) but have increased susceptibility to distraction, especially for unrelated task distractors (Costello et al., 2010; Reaves et al., 2016). Therefore, we suggest that meditation practice will impact firstly dealing with un-relevant external distractors (the most impacted process by aging), and eventually with longer practice, will positively affect the management of thoughts. To confirm this interpretation, our results should be compared with those of expert meditators, with the expectation that a beneficial effect of practice should also be observed for management of internal distraction. Moreover, it would also be interesting to compare older and younger novice populations to see if the effects of meditation training on the management of internal distractors differ across age groups. Regarding the absence of effect on the perceived cognitive difficulties (assessed by CDS; McNair & Kahn, 1983), we can hypothesize that the construct is too large (captures multiple cognitive processes) and maybe meditation only trained some of these processes (attentional for example). Another explanation would be that the perceived cognitive difficulties are indicative of an underlying disease process occurring (e.g., Alzheimer's disease). Therefore, we might not expect that meditation would impact disease-related cognitive concerns since it does not appear to alter Alzheimer's disease related biological processes (Chételat et al., 2022). Finally, our sample exhibits a relatively high level of education, and it is widely recognized that individuals with a high cognitive reserve, which includes higher education, tend to a lower cognitive decline with aging (Reuter-Lorenz and Park, 2014). Nevertheless, people with higher education may report more cognitive complaints (Narbutas et al., 2021), that was explained by better perception of their abilities and a higher focus on their cognitive efficiency. Moreover, they could also use compensatory strategies which could explain the absence of cognitive difficulties measured objectively (Narbutas et al., 2021; Stern et al., 2018). Our intervention protocol was not designed to investigate the influence of education on the relationships between subjective and objective cognition. However, level of education was systematically considered in our analyses. Furthermore, other protective factors inherent in cognitive reserve could have influenced the outcomes. While exploratory analyses considered anxiety and depression, it is noteworthy that factors like social interactions and daily activities could also impact cognition. Despite the implementation of two active intervention groups to control for the influence of social interactions during interventions, other extraneous activities might still affect our results. Indeed, Felisatti et al. (2023) showed, in the same sample, relationships with late-life cognitive activities and late-life experiences and objective cognition. However, little is known regarding associations between these variables and subjective cognition.

Interestingly, the effect of meditation and non-native language learning interventions on cognition differs according to whether objective or subjective measures of cognition are assessed. In another analysis of the data from the Age-Well RCT trial, Demnitz-King et al. (2023) did not observe difference between groups on the evolution of objective cognition while we observed here that the meditation training group reported a better management of distraction compared to non-native language training and to no intervention. Therefore, we may consider that meditation training (and more particularly mindfulness) promotes both attentional regulation (Lutz et al., 2008) and implementation of cognitive control (Incagli et al., 2020) that could lead to the perception of better management of some aspects of cognitive functioning. Moreover, the observation of a positive effect of meditation learning on perception of better attentional functioning, in absence of objective changes in performance may be explained by a low sensibility of cognitive tests for subtle cognitive improvement. Future analyses on follow-up data (around 36 months after the end of the intervention) will be needed to determine if a perception of a better management of external stimuli is maintained in the meditation group and if objective changes in cognition are observed later and predicted by subjective perception of attentional improvement observed here (Dufouil et al., 2005). Moreover, other studies would be worth conducting on the effect on subjective and objective measures of cognition in order to confirm the current findings and to emphasize the difference between performance-based and self-reported measures of cognition.

This longitudinal and randomized controlled trial (Poisnel et al., 2018) contributes causal evidence on the impact of 18 months of meditation training and non-native language training on subjective cognition in old age (Poisnel et al., 2018). Furthermore, this study on subjective cognition complements the objective cognition results that we have previously reported (Demnitz-King et al., 2023) in the understanding of older people's cognition. The use of questionnaires could better reflect their functioning in everyday life than laboratory tasks. We have, however, identified the following limitations. First, it was not possible to compare the distinct effect of mindfulness or compassion meditation training here because questionnaires about subjective cognition were not administered at 9 months, before compassion teaching became a main topic in the program. Future studies are needed to determine if the better management of external interference is more particularly associated with one of these two processes. Second, we used various scales that have been validated in existing literature, but we have not calculated internal consistencies specific to our population.

In conclusion, we observed an effect of meditation training on perceived external stimuli management. While no effect was observed on cognitive performance in a previous analysis of the same trial (Demnitz-King et al., 2023), meditation appears a helpful strategy to suppress external distractors and facilitate focus on specific tasks. These results suggest that subjective assessment of cognitive functioning may be useful to complement understanding of task-related performance changes in cognitive aging and the specific effect of interventions.

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Declaration of interest statement

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Data availability statement

The data are available upon request.

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Tables

Table 1. Demographic data at baseline and variables related to the intervention

Variables of interest	Meditation group (N=45)	Non-native language training group (N=45)	No intervention group (N=45)
Age (years), *Mean ± SD [range]*	69.45 ± 3.70 [65.0-78.4]	70.34 ± 4.50 [65.0 – 83.9]	68.13 ± 2.76 [65.0-76.4]
Years of education, *Mean ± SD [range]*	13.11 ± 3.07 [7.0-2.0]	12.16 ± 3.02 [7.0-17.0]	14.20 ± 2.88 [7.0-20.0]
Sex (female), *n (%)*	31 (69%)	25 (56%)	27 (60%)
Brain amyloid load (SUVR), *Mean ± SD [range]*	1.26 ± 0.16 [1.0-1.7] [1]	1.27 ± 0.19[1.1-1.8]	1.21 ± 0.09 [1.0-1.5]
APOE (ε4 positive), *n (%)[range]*	13/45 (28.9%)	12/45 (26.7%)	11/44 (25%)
STAI B delta score, *Mean ± SD [range]*	-0.07 ± 0.69 [-1.99-1.28] [1]	0.06 ± 1.03 [-2.85-2.56]	-0.14 ± 0.61 [-1.28-1.28]
GDS delta score, *Mean ± SD [range]*	0.23 ± 1.10 [-2.29-2.86] [1]	0.39 ± 0.97 [-1.72-2.29]	-0.16 ± 0.84 [-2.86-1.15]

Note. SD: Standard Deviation, APOE: Apolipoprotein E, STAI B: State-Trait Anxiety Inventory – Trait version; GDS: Geriatric Depression Scale. Amyloid: brain amyloid load (standard uptake value ratios were acquired with late Florbetapir-PET), [1]N=44.

Table 2. Descriptive statistics of variables of interest (Cognitive Difficulties Scale and Attentional Style Questionnaire: global, internal and external scores)

	Meditation group (N=45)		**Non-native language training group (N=45)**		**Control group (N=45)**	
Variables of interest	**Baseline**	**Post-intervention**	**Baseline**	**Post-intervention**	**Baseline**	**Post-intervention**
CDS Total score *(Mean ± SD)*	32.64 ± 14.66	31.47 ± 16.49	35.49 ± 16.40	36.76 ± 16.65	33.09 ± 14.19	33.77 ± 14.98 [1]
ASQ Internal score *(Mean ± SD)*	21.07 ± 4.90 [1]	20.56 ± 4.67	20.38 ± 4.46	20.84 ± 4.71	20.27 ± 4.65 [1]	19.68 ± 4.40 [1]
ASQ External score *(Mean ± SD)*	16.05 ± 5.50 [1]*	14.24 ± 5.24*	16.73 ± 3.82	16.60 ± 3.23	15.73 ± 4.09 [1]	15.50 ± 4.25 [1]

Note. SD: Standard Deviation, [1]N=44, CDS: Cognitive Difficulties Scale, ASQ : Attentional Style Questionnaire, * significant difference through time.

Table 3. Differences in variables related to the intervention

Variables of interest	Meditation group (N=45)	Non-native language training group (N=45)
Practice (number of minutes of home and class practice), *Mean ± SD [range]*	17971.33 ± 9633.29 [17652.55 - 40012.5]	18072.56 ± 8077.56 [1492.5 - 46170.0]
Adherence (% of class attendance), *Mean ± SD [range]*	60.64 ± 8.19 [26.0 – 70.0]	58.07 ± 12.27 [7.0 – 68.0]
Responsiveness (responders), *n (%)*	38/45 (84%)	43/45 (96%)
Credibility, *Mean ± SD [range]*	-0.10 ± 0.96 [-2.5 - 1.1]	0.07 ± 1.04 [-3.6 - 1.1]
Expectancy, *Mean ± SD [range]*	0.13 ± 0.89 [-1.9 – 1.7]	-0.12 ± 1.10 [-3.2 – 1.7]

Note. SD: Standard Deviation. Practice, adherence and responsiveness measures correspond to the involvement of participants in the intervention. Credibility and expectancy refer to the credibility associated with the intervention, and expectancies of the participants after participation in the first session, * between-group difference.

Table 4. Core models (group differences, controlled for education, age, gender and baseline scores)

Predictors	**Estimate (95% CI)**	**F (df)**	***p***
A. CDS total score			
Group	/	1.23 (2, 127)	.30
Meditation training vs non-native language training	-0.001 (-0.33, 0.33)	/	/
Meditation training vs no intervention	-0.20 (-0.53, 0.14)	/	/
Non-native language training vs no intervention	-0.19 (-0.55, 0.15)	/	/
Education	-0.02 (-0.06, 0.02)	1.09 (1, 127)	.30
Age	**0.04 (0.01, 0.07)**	**5.55 (1, 127)**	**.02 (R_{sp}^2=.04)**
***Gender** (female vs male)*	-0.07 (-0.31, 0.17)	0.36 (1,127)	.55
Baseline CDS total score	**-0.01 (-0.02, -0.005)**	**10.03 (1,127)**	**.002 (R_{sp}^2=.07)**
B. ASQ internal score			
Group	/	0.41 (2,125)	.66
Meditation training vs non-native language training	-0.14 (-0.54, 0.26)	/	/
Meditation training vs no intervention	-0.01 (-0.42, 0.39)	/	/

Non-native language training vs no intervention	0.13 (-0.29, 0.55)	/	/
Education	-0.02 (-0.07, 0.03)	0.56 (1,125)	.46
Age	0.03 (-0.004, 0.07)	3.20 (1,125)	.08
Gender *(female vs male)*	0.10 (-0.19, 0.38)	0.45 (1,125)	.50
Baseline ASQ internal score	**-0.09 (-0.12, -0.06)**	**33.54 (1,125)**	**<.0001 (R_{sp}^2=.21)**

C. ASQ external score

Group	/	**4.84 (2,125)**	**<.01 (R_{sp}^2=.07)**
Meditation training vs non-native language training	**-0.37 (-0.69, -0.05)**	/	/
Meditation training vs no intervention	**-0.34 (-0.66, -0.02)**	/	/
Non-native language training vs no intervention	0.03 (-0.31, 0.36)	/	/
Education	-0.03 (-0.07, 0.01)	2.29 (1,125)	.13
Age	-0.01 (-0.04, 0.02)	0.24 (1,125)	.63
Gender *(female vs male)*	0.10 (-0.13, 0.32)	0.71 (1,125)	.40
Baseline ASQ external score	**-0.07 (-0.09, -0.04)**	**29.42 (1,125)**	**<.0001 (R_{sp}^2=.19)**

Note. N=132, CI: Confidence Interval, df: degrees of freedom, R_{sp}^2: semi-partial R^2, CDS: Cognitive Difficulties Scale, Tukey-Cramer correction for 95% CI of the group effect. For all analyses, education, age, gender and baseline outcome data were used as covariates.

Supplemental Material - "The evolution of subjective cognition after meditation training in older people: A secondary analysis of the three-arm Age-Well randomized controlled trial"

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Appendix I. The Medit-Ageing Research Group

Many thanks to: Florence Allais, Claire André, Eider Arenaza-Urquijo, Julien Asselineau, Nicholas Ashton, Romain Bachelet, Sebastian Baez Lugo, Thorsten Barnhofer, Martine Batchelor, Axel Beaugonin, Alexandre Bejanin, Viviane Belleoud, Clara Benson, Beatriz Bosch, Maelle Botton, Maria Pilar Casanova, Pierre Champetier, Anne Chocat, Nina Coll-Padros, Rowane Coueron, Sophie Dautricourt, Robin De Flores, Vincent De La Sayette, Pascal Delamillieure, Marion Delarue, Yacila Deza-Araujo, Stéphanie Egret, Hélène Espérou, Francesca Felisatti, Eglantine Ferrand Devouge, Antoine Garnier-Groussard, Francis Gheysen, Karine Goldet, Idir Hamdidouche, Marc Heidmann, Thien Huong Tran, Abdul Hye, Frank Jessen, Agathe Joret Philippe, Olga Klimecki, Pierre Krolak Salmon, Elizabeth Kuhn, Renaud La Joie, Brigitte Landeau, Gwendoline Le Du, Valérie Lefranc, Maria Leon, Dix Meiberth, Florence Mezenge, Ester Milz, Jose Luis Molinuevo, Inès Moulinet, Hendrik Mueller, Theresa Mueller, Valentin Ourry, Cassandre Palix, Léo Paly, Stephano Poletti, Anne Quillard, Alfredo Ramirez, Géraldine Rauchs, Stéphane Rehel, Leslie Reyrolle, Laura Richert, Ana Salinero, Raquel Sanchez, Lena Sannemann, Yamna Satgunasingam, Ann-Katrin Schild, Corinne Schimmer, Christine Schwimmer, Siya Sherif, Hilde Steinhauser, Clémence Tomadesso, Edelweiss Touron, Matthieu Vanhoutte, Denis Vivien, Patrik Vuilleumier, Cédrick Wallet, Caitlin Ware, Janet Wingrove and Miranka Wirth.

Appendix II. Additional measures

Other details on these additional measures can be found in Demnitz-King et al. (2023).

- **Brain amyloid load**:

The amyloid standard uptake value ratios correspond to late (50-60min) Florbetapir-PET acquisition: Amyvid (AV45) solution for injection of 4MBq/kg, 47 slices 2.7x2.7x3.27mm³.

- **Apolipoprotein genotype**:

Participants were considered as ε4 positive when they had at least one ε4 allele (i.e., ε2/ ε4, ε3/ ε4 or ε4/ ε4), and ε4 negative when no ε4 allele (i.e., ε2/ ε3 or ε3/ ε3).

- **Credibility and Expectancy Questionnaire**:

This questionnaire from Devilly & Borkovec (2000) measures the credibility the participant confers to the intervention and the expectancies he has about the outcomes. This scale is composed of 6 items: three questions for the credibility factor (Cronbach's α = between 0.81 and 0.86), and three for the expectancy factor (Cronbach's α = between 0.79 and 0.90) (Devilly & Borkovec, 2000). Each question is Z-scored based on the distribution of baseline values, then averaged for each factor. Scores are then Z-transformed again to create composite scores for credibility and expectancy, with higher scores indicating higher levels of credibility and expectancy.

- **Waves in which participants were included**:

There were three inclusion waves in the study (43 participants in the first one, 50 in the second one and 44 in the third one) corresponding to three periods of 3 months recruitment.

- **Adherence**:

It corresponds to the percentage of class attendance and was rated by the teachers.

- **Practice**:

It corresponds to the number of hours when the participant practiced meditation or learned English during classes and at home. It was rated by the participant himself.

- **Responsiveness**:

Across both intervention groups, whether, and the degree to which participants responded to their assigned intervention was assessed. Specifically, a **dichotomous categorical variable** classifying participants as either intervention 'responders' or 'non-responders', and a **continuous measure** of responsiveness were computed.

1) The **categorical score** (responder or non-responder) made the distinction between those who responded to the intervention and those who did not.
   a. For the meditation training group, it was based on the teachers' opinion regarding the participant's evolution (Likert scale from 0 "not at all" to 5 "a lot" with participants having scores of 0 or 1 ["very few"] considered as non-responders).
   b. For the non-native language training group, the score was created based on two scores: teacher's opinion on the same Likert scale than previously presented and results on an English test. Participants who were given a score of 0 or 1 by the teachers – and had an improvement of less than one point to the English test for the non-native language training group – were deemed to be non-responders.
2) The **continuous score** combined different standardized scores.
   a. For the meditation training group, three scores were used. First, a score of

change (post-intervention minus pre-intervention) on a global meditation composite score was calculated based on results on meditation questionnaires (see Schlosser et al., 2022 for more details). Second, we used scores related to the perception of intervention responsiveness rated by the teachers (as in point 1) and another 5-Likert scale of their perception of the levels of connection, positive emotions, negative emotions, and meta-awareness of the participant. Third and finally, we considered scores related to the perception of intervention responsiveness rated by the participant on the same scale that presented in point 1 regarding both meditation sessions and daily life. The sub-scores of the meditation score were first standardized using relative means and standard deviation, and second were averaged into one score. The sub-scores of the teacher's rating were also first standardized using the relevant means and standard deviations and then averaged. The same procedure was applied for the sub-scores of the participant's rating. These three domain scores (global meditation score, teacher's perception and participant's perception) were each standardized again. The three standardized domain scores were then averaged and re-standardized to create the final responsiveness variable, with a mean of 0 and standard deviation of 1.

b. For the non-native language training group, the final score was composed of two sub-scores: the change on a score obtained on an English test and the perception of intervention responsiveness rated by the teachers as in point 1. Both domain scores (score on the English test and score on the question given to the teachers) were first standardized using the relevant means and standard deviations. The two standardized domain scores were then averaged and re-standardized create the final responsiveness variable, with a mean of 0 and standard deviation of 1.

- **<u>State-Trait Anxiety Inventory (STAI)</u>**:

This questionnaire from Spielberger et al. (1970) measures the level of anxiety of the participant. There are two subscales: STAI-trait (STAI B, Cronbach's α = 0.90) which measures the global anxiety of the participant and the STAI-state (STAI A, Cronbach's α = 0.93) which measures the anxiety felt by the participant at the present moment (Skapinakis, 2014). Each subscale is composed of 20 items. The score of each subscale varies from 20 (low level of anxiety) to 80 (high level of anxiety). The standardized delta score (post- minus pre-test scores / standard deviation of pre-test scores) of the STAI-trait (STAI-B) was calculated and used in the analyses.

- **<u>Geriatric Depression Scale (GDS)</u>**:

This questionnaire from Yesavage (1988) measures the level of depression of the participant. This is a 15-item scale (Cronbach's α = 0.92) and the score varies from 0 (low level of anxiety) to 15 (high level of anxiety) (Durmaz et al., 2018). The standardized delta score (post- minus pre-test scores / standard deviation of pre-test scores) was calculated and used in the analyses.

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Supplemental Table 1. Raw data for anxiety and depression scales

Variables of interest	**Whole sample (N=135)**	**Number of people above the cut-off values**
STAI B raw pre-score, *Mean ± SD*	34.55 ± 7.02	**Moderate anxiety** (score>37): 34/135 (25.19%) **High anxiety** (score>44): 12/135 (8.89%)
GDS raw pre-score, *Mean ± SD*	1.28 ± 1.75	**Mild depression** (score>9): 1/135 (0.74%) **Severe depression** (score>19): 0/135 (0%)

Note. SD: Standard Deviation.

Supplementary table 2. Mixed model analyses with i) anxiety as covariate, ii) depression as covariate, iii) with a sample with more than 20% of adherence to the intervention (in comparison with no-intervention), with the responders to the intervention (in comparison with no-intervention)

		i) Anxiety as covariate	ii) Depression as covariate	iii) Adherence > 20%	iv) Subsample of responders
Group effect on CDS delta score, *estimate (95% CI)*	*Meditation training vs non-native language training*	-0.02 (-0.36, 0.32)	-0.01 (-0.35, 0.32)	-0.04 (-0.38, 0.30)	0.01 (-0.35, 0.38)
	Meditation training vs no intervention	-0.16 (-0.50, 0.18)	-0.21 (-0.55, 0.14)	-0.16 (-0.50, 0.19)	-0.12 (-0.48, 0.24)
	Non-native language training vs no intervention	-0.14 (-0.49, 0.22)	-0.19 (-0.55, 0.17)	-0.12 (-0.47, 0.24)	-0.13 (-0.49, 0.23)
Group effect on ASQ delta internal score, *estimate (95% CI)*	*Meditation training vs non-native language training*	-0.13 (-0.53, 0.27)	-0.14 (-0.54, 0.26)	-0.14 (-0.54, 0.27)	-0.21 (-0.64, 0.22)
	Meditation training vs no intervention	-0.02 (-0.42, 0.39)	-0.02 (-0.43, 0.39)	-0.01 (-0.42, 0.40)	-0.09 (-0.51, 0.34)
	Non-native language training vs no intervention	0.11 (-0.31, 0.54)	0.12 (-0.32, 0.55)	0.12 (-0.30, 0.55)	0.12 (-0.30, 0.55)
Group effect on ASQ delta external score *estimate (95% CI)*	*Meditation training vs non-native language training*	**-0.36 (-0.69, -0.05)**	**-0.37 (-0.69, -0.05)**	**-0.37 (-0.69, -0.05)**	**-0.36 (-0.70, -0.02)**
	Meditation training vs no intervention	**-0.35 (-0.67, -0.02)**	**-0.35 (-0.67, -0.02)**	**-0.34 (-0.66, -0.02)**	-0.34 (-0.68, 0.002)
	Non-native language training vs no intervention	0.02 (-0.32, 0.37)	0.02 (-0.32, 0.37)	0.03 (-0.31, 0.37)	0.02 (-0.32, 0.37)

Note. CI: Confidence Interval, CDS: Cognitive Difficulties Scale, Tukey-Cramer correction for 95% CI of the group effect. Adjusted for education, age, gender and baseline outcome data.

Supplementary table 3. Mixed model analyses with different predictors

Predictor	Estimate (95% CI)					
	Meditation training			Foreign language training		
	CDS	ASQ internal	ASQ external	CDS	ASQ internal	ASQ external
Age	0.002 (-0.05, 0.06)	-0.02 (-0.08, 0.05)	-0.05 (-0.11, 0.01)	**0.02 (0.01, 0.08)**	**0.07 (0.02, 0.12)**	0.01 (-0.03, 0.05)
Sex [1]	0.02 (-0.49, 0.52)	0.06 (-0.48, 0.61)	0.25 (-0.22, 0.71)	-0.21 (-0.56, 0.15)	-0.07 (-0.51, 0.37)	0.20 (-0.14, 0.53)
Education	-0.01 (-0.08, 0.07)	-0.06 (-0.15, 0.02)	-0.02 (-0.10, 0.06)	-0.07 (-0.03,0.06)	0.04 (-0.04, 0.11)	-0.003 (-0.06, 0.05)
Baseline score	-0.01 (-0.03, 0.01)	**-0.10 (-0.15, -0.04)**	**-0.06 (-0.10, -0.02)**	-0.01 (-0.02, 0.0001)	-0.03 (-0.08, 0.02)	**-0.09 (-0.13, -0.04)**
APOE [2]	-0.11 (-0.62, 0.41)	-0.21 (-0.76, 0.34)	-0.17 (-0.67, 0.34)	0.21 (-0.18, 0.59)	-0.11 (-0.60, 0.38)	-0.13 (-0.49, 0.24)
Amyloid	**1.87 (0.52, 3.22)**	-1.21 (-2.82, 0.40)	1.00 (-0.39, 2.38)	0.39 (-0.55, 1.33)	0.18 (-1.03, 1.38)	0.29 (-0.62, 1.19)
Credibility	-0.01 (-0.29, 0.26)	-0.03 (-0.33, 0.26)	-0.05 (-0.31, 0.22)	-0.06 (-0.25, 0.14)	0.18 (-0.04, 0.41)	0.003 (-0.17, 0.18)
Expectancy	-0.04 (-0.31, 0.23)	-0.20 (-0.48, 0.09)	-0.001 (-0.26, 0.26)	-0.12 (-0.29, 0.05)	**0.21 (0.01, 0.40)**	-0.11 (-0.27, 0.05)
Adherence	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.02)	0.02 (-0.004, 0.05)	0.005 (-0.01, 0.02)	0.001 (-0.02, 0.02)	-0.0001 (-0.01, 0.01)
Wave [3]						
Wave 2	-0.25 (-0.82, 0.32)	-0.03 (-0.65, 0.60)	0.47 (-0.06, 0.99)	0.29 (-0.13, 0.71)	-0.30 (-0.89, 0.28)	-0.17 (-0.62, 0.28)
Wave 3	0.16 (-0.44, 0.77)	0.05 (-0.58, 0.67)	0.47 (-0.05, 0.99)	0.09 (-0.31, 0.49)	-0.04 (-0.56, 0.49)	-0.17 (-0.56, 0.23)
Practice	-0.00002 (-0.00005, 0.000004)	-0.00001 (-0.00003, 0.00002)	0.00001 (-0.00002, 0.00003)	-0.000003 (-0.00003, 0.00001)	-0.000002 (-0.00004, 0.00001)	-0.0000002 (-0.00002, 0.00002)
Responsiveness	-0.16 (-0.40, 0.08)	-0.10 (-0.37, 0.16)	-0.04 (-0.28, 0.20)	0.03 (-0.15, 0.20)	-0.06 (-0.29, 0.17)	-0.02 (-0.19, 0.15)

Note. Estimates and confidence intervals (CI 95%) of the different predictors with age, gender, education and baseline data as covariates. **Significant results (p<.05) in bold.** CDS: Cognitive Difficulties Scale, ASQ: Attentional Style Questionnaire, CI: Confidence intervals, APOE: Apolipoprotein E), [1] Reference sex is male. [2] Reference APOE genotype is no ε4 allele. [3] Reference wave is the first wave).